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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/625,854 | 07/23/2003 | Andre Delacourte | 11362.0039.NPUS01 | 9442 |

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| EXAMINER | |
|---|---|
| WANG, CHANG YU | |
| **ART UNIT** | **PAPER NUMBER** |
| 1649 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 01/08/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| **Advisory Action Before the Filing of an Appeal Brief** | **Application No.** 10/625,854 | **Applicant(s)** DELACOURTE ET AL. | |
|---|---|---|---|
| | **Examiner** Chang-Yu Wang | **Art Unit** 1649 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 21 December 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *26,35,37,40,41,43,57-61 and 64*.
   Claim(s) withdrawn from consideration: *37*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
    See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud

/CYW/

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's amendment and arguments are insufficient to overcome the rejection under 35.U.C.C 112, 1st paragraph, lack of scope of enablement and the rejectioin under 35.U.S.C. 112, 2nd paragraph, indefiniteness for the reasons previously made of record.
Claims 26, 35, 36, 40-43, 57-61, 63 and 64 stand under 35.U.C.C 112, 1st paragraph, lack of scope of enablement. At p. 5-6 of the response, Applicant argues that the claims are enabled because instant claim 26 has been amended to recite Alzheimer's disease and the specification provides findings of detection different modified Abeta42 variants in patients suffering from different forms of AD. Applicant's arguments have been fully considered but they are not persuasive. In contrast, as previously made of record, the guidance provided within the specification does not reasonably extrapolate to a method for aiding in the determination of whether a patient is susceptible to or at risk of Alzheimer's disease as recited in instant claims 26, 35, 36, 40-43, 57-61, 63 and 64. Applicant is not enabled for the claimed method without specific knowledge of the expression profile of specific Abeta variants that are present in patients known not to suffer from the disease because different Abeta variants can be detected in CSF of patients suffering from AD (i.e. patients have been diagnosed with a specific AD or amyloid-associated disorders) and S0 controls or other controls. The detection of different Abeta variants in different status of patients could be false positive or false negative, in particular Abeta 8-42 or Abeta 4-42 or Abeta 5-42 as discussed in the previous office action, as shown in the specification and as evidenced by Applicant's declaration. Thus, it is unclear which Abeta variants and what expression levels of specific Abeta variants can be used as a marker to determine whether a naïve person is susceptible to or at risk of AD. In addition, Applicant fails to provide a standard expression profile of Abeta variants in controls known not to suffer from AD. It is unpredictable what expression levels and what specific species of Abeta variants can be measured and used to determine whether a person is susceptible to or at risk of the disease.

Claims 26, 35, 36, 40-43, 57-61, 63 and 64 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite because of the recitation "greater" in the instant claims. At p. 4-5 of the response, Applicant argues that the term "greater" has been used in several issued patents so it is not indefinite. It is noted that each application is judged by its own merits. In addition, in contrast, the instant specification does not provide a standard for ascertaining the requisite degree so one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant fails to set forth the metes and bounds of what is encompassed within the definition of "greater". Based on the disclosure in the specification, a skilled artisan cannot determine what amount of the expression of Abeta variants and what specific Abeta variants would be in controls vs. in patients susceptible to or at risk of a disease associated with amyloid formation and aggregation as recited in the claims. Thus these claims are indefinite.

/CYW/
1/3/07

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